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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/750,972	12/28/2000	Pramod K. Srivastava	8449-134	7769

20583 7590 06/05/2002

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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	15

DATE MAILED: 06/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/750,972	SRIVASTAVA, PRAMOD K.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *75 and 97-128* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *75 and 97-128* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9 &14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group III in Paper No. 13 is acknowledged. Claims 1-74, 76-96 have been canceled without prejudice, claims 97-128 have been newly added. Claims 75, 97-128 are examined on the merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 75, 97-128 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for alpha 2 marcoglobulin (α2M) and anti-CD91 antibody (α2M receptor antibody), does not reasonably provide enablement for any purified compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. OK

The instant application is drawn to methods of treating and preventing diseases or disorders, cancer, infectious diseases, and autoimmune disorders by utilizing a purified compound that is capable of either binding to α2M receptor, or modulates the interaction of α2M receptor with a heat shock protein/ α2M receptor ligand. Although the instant application is enabled for the use of α2M or an anti-CD91 antibody, it is virtually silent in regards to any other purified compound that is capable of performing

such actions. Because the instant application is silent in this regard, it forces the skilled artisan to experiment.

The factors which must be considered in determining undue experimentation are set forth in *In re Wands* 8 USPQ2d 1400. The factors include: (1) quantity of experimentation, (2) the amount of guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the predictability of the art and, (7) breadth of the claims.

With regards to factors one and two cited above, the quantity of experimentation needed to determine which compounds are capable of modulating or binding to the α2M receptor is high, because the skilled artisan would not know where to initiate his/her search for such compounds. The instant specification has only provided the skilled artisan the starting materials of heat shock proteins, α2M, and antibodies.

With regards to factors four, five and six cited above, it is noted that there is a great deal of unpredictability associated with treating or preventing diseases such as cancer, infectious diseases and autoimmune diseases. For example, **Gura** (Ref) shows that not all methods for screening and testing for cancer compounds are effective and that problems are often found during the translation between animal models to humans. The instant specification fails to provide a specific methodological procedure for the identification or the use of nay other compound aside from α2M, and antibodies to α2M receptor/CD91.

With regards to factors three and six cited above, it is noted that the working examples are limited to the identification of the interaction between α2M receptor and

heat shock proteins and the induction of an immune response. Such is not seen as sufficient to support the breadth of the claims, wherein the claims recite the use of any purified compound that either binds to α2M receptor or modulates the interaction between α2M receptor and heat shock proteins.

4. Claims 97,98,102, 115,117,126 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for gp96, HSP70, and HSP90, does not reasonably provide enablement for all heat shock protiens. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification is drawn to a method of treating or preventing diseaseor diseases comprising administration of a purified compound that modulates the interaction between α2M receptor and heat shock protein, where the compound binds to HSPs or is an antibody specific for HSPs. Because the instant specification is silent to the use of any other HSP, other than gp96, HSP70 and HSP90, it would force the skilled artisan to experiment to determine which other HSP can be used to performed the invention as claimed.

With regard to factors one and two cited above, the quantity of experimentation needed to determine which other HSP are capable of performing the same function as those disclosed in the instant application, there has not been provided adequate guidance in the written description for accomplishing and determining such.

With regards to factors four, five, and six cited above, it is noted that there is a great deal of unpredictability associated with the treatment of cancer, infectious

diseases, and autoimmune diseases through the use of HSP other than gp96, HSP70, and HSP90. Srivastava P (Nature Rev Immunol 2002 Mar; 2(3); 185-94) discloses that HSP are the most abundant intracellular proteins, and that they perform a multitude of functions in the cell. Therefore, it is possible that not all HSP perform the same function as disclosed in the instant specification. In addition, the instant specification does not describe any specific methodological steps associated with any other HSP that are intended to be used for treating any disease.

With regard to factors three and seven cited above it is noted that the working examples are limited to three HSPs, namely gp96, HSP70, and HSP90. Such is not seen as adequate to encompss the breadth of the claims, wherein the claims recite any and all HSPs.

5. Claim 121 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 121 is drawn to a method of treating or preventing disease through the administration of a purified compound, wherein the purified compound is an agonist of α2M receptor. The applicant has not provided to the public the evidence that the applicant was in possession of said claimed invention at the time of filing. The specification does not provide any evidence of or recite any specific utility of any agonist that is capable of binding or modulating the interaction between α2M receptor and its ligand.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 75,97,104,105,107,108,110,111,113,122, and 123 are rejected under 35 U.S.C. 102(b) as being anticipated by Pizzo S (WO 94/14976; **IDS** DK). Pizzo S. discloses of a method of treating or preventing infectious diseases, autoimmune disease, or cancer, by administering a compound that binds to α2M receptor and modulates the activity of the α2M receptor. Furthermore, Pizzo S. contemplates the use of antagonists because Pizzo S. discloses the use of antibodies capable of binding to the α2M receptor. Inherently, these antibodies are therefore antagonist to the receptor. Therefore, the claims as recited are anticipated.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 75, 97,103-114, 116, 122, 123, and 127 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pizzo S. (WO 94/14976; **IDS** DK) in view of Isaacs *et al.* (J. Biol Chem 1988 May;263(14):6709-6714; **IDS** EF).

Pizzo S. discloses of a method of treating or preventing infectious diseases, autoimmune diseases, and cancer. Pizzo S. further discloses the use of antibodies for said methods, wherein the antibody associates with the α2M receptor. Pizzo S does not however, disclose of purified compounds that interact with the ligand of α2M receptor. Isaac *et al.* however do disclose of compounds that specifically interact with the α2M receptor binding domain on α2M. The disclosed compound is an anti idiotypic antibody capable of inhibiting the interaction between α2M receptor and α2M.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to conceive of a method of treating cancer, autoimmune disease, or infectious disease, using a purified compound that either binds or modulates the interaction between α2M and its ligand, because the prior art provides sufficient motivation to practice the invention as claimed. The suggestion/motivation for doing what the applicant has claimed is that it was already known in the art that a method for

preventing cancer, autoimmune diseases, and infectious diseases by interrupting or modulating the interaction between α2M receptor and its ligand existed. It was also known that antibodies to α2M, a ligand for α2M receptor was available and effective in inhibiting the interaction between α2M and α2M receptor. It would have been *prima facie* obvious at the time of the invention to combine the references because if blocking the receptor was an effective method of inhibiting the diseases claimed, then an antibody that inhibited a ligand to the receptor would also be very effective.

Conclusion

No claims allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christophr Yaen
Art Unit 1642
May 28, 2002

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